

Rec'd PCT/PPO 06 JUL 2005

54/555

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization International Bureau



(43) International Publication Date
28 October 2004 (28.10.2004)

PCT

(10) International Publication Number
WO 2004/092131 A1

(51) International Patent Classification⁷: C07D 209/08, 209/42, 405/12, 409/12, 413/12, 413/14, 417/06, 417/12, 417/14, A61K 31/404, 31/422, 31/427, 31/4402, 31/4409, 31/5377, A61P 3/10, 29/00

ZHU, Guoxin [CN/US]; Noblesville, IN (US). SCHKERYANTZ, Jeffrey, Michael [US/US]; Fishers, IN (US). MICHELLYS, Pierre-Yves [FR/US]; 10824 Poblado Road, No. 221, San Diego, CA 92127 (US).

(21) International Application Number:
PCT/US2003/041698

(74) Agents: DAVIS, Steven, G. et al.; Hamilton, Brook, Smith & Reynolds, P.C., 530 Virginia Road, P.O. Box 9133, Concord, MA 01742-9133 (US).

(22) International Filing Date:
31 December 2003 (31.12.2003)

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/438,541 6 January 2003 (06.01.2003) US

(84) Designated States (*regional*): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(72) Inventors; and

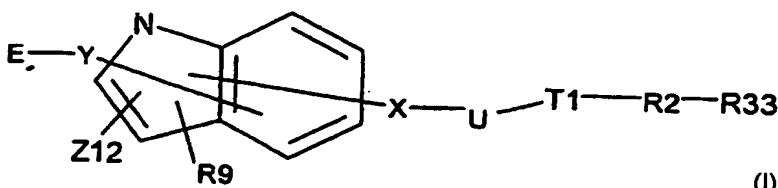
Published:

(75) Inventors/Applicants (for US only): CONNER, Scott, Eugene [US/US]; Elizabethtown, IN (US). KNOBELS-DORG, James, Allen [US/US]; Noblesville, IN (US). MANTLO, Nathan, Bryan [US/US]; Brownsburg, IN (US). MAYHUGH, Daniel, Ray [US/US]; Carmel, IN (US). WANG, Xiaodong [CN/US]; Carmel, IN (US).

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: INDOLE DERIVATIVES AS PPAR MODULATORS



(I)

(57) Abstract: The present invention is directed to a method of treatment by modulating a peroxisome proliferator activated receptor by employing a compound of Structural Formula (I). The variables in (I) are defined herein. Also included are compounds, methods of making compounds, and pharmaceutical compositions. The preventing Syndrome X, Type II diabetes, and cardiovascular diseases.

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compounds of the present invention are believed to be effective in treating and preventing Syndrome X, Type II diabetes, and cardiovascular diseases.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/41698

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07D209/08	C07D209/42	C07D405/12	C07D409/12	C07D413/12
	C07D413/14	C07D417/06	C07D417/12	C07D417/14	A61K31/404
	A61K31/422	A61K31/427	A61K31/4402	A61K31/4409	A61K31/5377

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/30895 A (BAYER AG) 18 April 2002 (2002-04-18) claims 1,2,26-28,33-35,38-60; examples 220,240,241,261,273,283,284,287-299,301,34 3,344 ---	1-140
X	WO 01/30343 A (BERGER JOEL P ;VENTRE JOHN (US); ZHANG BEI B (US); LEIBOWITZ MARK) 3 May 2001 (2001-05-03) page 6, line 16 -page 10, line 12; claims ---	1-140
Y	US 5 767 133 A (DOW ROBERT L ET AL) 16 June 1998 (1998-06-16) claims 1,48,49; examples 60,63,68,71,73,75,79,101,102,104,106,115,1 17 ---	1-140
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Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the International filing date
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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *8* document member of the same patent family

Date of the actual completion of the international search

7 May 2004

Date of mailing of the International search report

24/05/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Hanisch, I

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/41698

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 A61P3/10 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>RAMI H K ET AL: "Synthetic ligands for PPAR gamma - review of patent literature 1994-1999"</p> <p>EXPERT OPINION ON THERAPEUTIC PATENTS, ASHLEY PUBLICATIONS, GB, vol. 10, no. 5, 2000, pages 623-623, XP002257971</p> <p>ISSN: 1354-3776</p> <p>the whole document</p> <p>---</p>	1-140
P, X	<p>WO 03/074051 A (FILZEN GARY FREDERICK ; GEYER ANDREW GEORGE (US); CHENG XUE-MIN (US) 12 September 2003 (2003-09-12)</p> <p>abstract; claims 1-5,9-13,15; examples 21,24,25</p> <p>-----</p>	1-140

Further documents are listed in the continuation of box C.

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- *O* document referring to an oral disclosure, use, exhibition or other means
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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

7 May 2004

Date of mailing of the international search report

Name and mailing address of the ISA

European Patent Office, P.O. Box 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Hanisch, I

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 92-139 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.1

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 1-42,44-87,89-139(all part)

Present claim 1 and all claims referring back to the current general formula relate to an extremely large number of possible compounds thus encompassing known general formulae (and claim 92 additionally already exemplified compounds). Besides the unlimited expressions "aryl", "heteroaryl", "aliphatic linker" etc. which among others may all be optionally substituted (see description) in particular the undefined connectivities give rise to a very large number of alternatives. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of claims 43, 88 and 140, compositions containing the same and uses thereof, as well as the examples.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/41698

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: - because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. Claims Nos.: 1-42, 44-87, 89-139(all part) because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/41698

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
WO 0230895	A	18-04-2002	AU CA EP HU NO WO US	1190102 A 2427499 A1 1341761 A1 0302477 A2 20031619 A 0230895 A1 2003087902 A1		22-04-2002 18-04-2002 10-09-2003 29-12-2003 02-06-2003 18-04-2002 08-05-2003
WO 0130343	A	03-05-2001	AU CA EP JP WO US	1215701 A 2386750 A1 1284728 A1 2003525217 T 0130343 A1 2003032581 A1		08-05-2001 03-05-2001 26-02-2003 26-08-2003 03-05-2001 13-02-2003
US 5767133	A	16-06-1998	AU AU BR DE DE EP GR JP NO PL AT CA CN CZ DK ES FI HU WO NZ ZA	675536 B2 6687094 A 9406823 A 69404039 D1 69404039 T2 0703911 A1 3024134 T3 8506348 T 955047 A 312005 A1 154935 T 2164009 A1 1129443 A 9503277 A3 703911 T3 2104383 T3 942791 A 70844 A2 9429290 A1 265692 A 9404139 A		06-02-1997 03-01-1995 26-03-1996 07-08-1997 16-10-1997 03-04-1996 31-10-1997 09-07-1996 13-12-1995 01-04-1996 15-07-1997 22-12-1994 21-08-1996 14-08-1996 06-10-1997 01-10-1997 15-12-1994 28-11-1995 22-12-1994 24-02-1997 13-12-1995
WO 03074051	A	12-09-2003	WO US	03074051 A1 2003207915 A1		12-09-2003 06-11-2003